

Title of the study: *Clinical Validation of Artificial Intelligence in polyp detection*
Sponsor of the study: *University Hospitals Leuven, Herestraat 49, B-3000 Leuven*
Research organisation: *University Hospitals Leuven, Herestraat 49, B-3000 Leuven*
Medical Ethics Committee: *Medical Ethics Committee of the University Hospitals Catholic University Leuven, Campus Gasthuisberg, Herestraat 49, B-3000 Leuven*
Local investigators: *Prof. dr. Raf Bisschops, Department of Gastroenterology and Hepatology, University Hospitals Leuven, Campus Gasthuisberg, B-3000 Leuven*

I Information vital to your decision to take part

Introduction

You are being invited to take part in a clinical study to evaluate a medical device with diagnostic purposes.

The sponsor and investigator hope that this medicinal product may offer advantages in patients who undergo a colonoscopy. There is, however, no guarantee that you will benefit from taking part in this study.

Before you agree to take part in this study, we invite you to take note of its implications in terms of organisation, possible risks and benefits, to allow you to make a decision with full awareness of the implications. This is known as giving “informed consent”.

Please read these few pages of information carefully and ask any questions you want to the investigator or his/her representative. There are 3 parts to this document: the information essential to your decision, your written consent and supplementary information (appendices) detailing certain aspects of the basic information.

If you take part in this clinical study, you should be aware that:

- This clinical study is being conducted after having been reviewed by one or more ethics committees.
- Your participation is voluntary and must remain free from any coercion. It requires the signature of a document expressing your consent. Even after having signed this document, you can stop taking part by informing the investigator. Your decision not to take part or to stop taking part in the study will have no impact on the quality of your care or on your relationship with the investigator.
- The data collected on this occasion are confidential and your anonymity is guaranteed during publication of the results.
- Insurance has been taken out in case you should suffer any damage in connection with your participation in this clinical study.
- You may contact the investigator or a member of his/her team at any time should you need any additional information.

Further information about your “Rights as a participant in a clinical study” can be found in appendix III.3.

Objectives and description of the study protocol

We are inviting you to take part in a clinical study involving the use of a new artificial intelligence tool for colonic polyp detection that is to include around 1500 patients, including approximately 250 in Belgium.

This study has been organised to further clinically validate a new artificial intelligence (AI) tool for colonic polyp detection during standard colonoscopy and to evaluate its clinical feasibility in daily practise. In addition, we want to use the obtained data for further development of an AI tool for characterization of colonic polyps.

To be able to take part in this study you must meet the following inclusion criteria:

- Age at least 18 years old
- Referral for screening, surveillance or diagnostic colonoscopy
- Able to give informed consent by the patient or by a legal representative

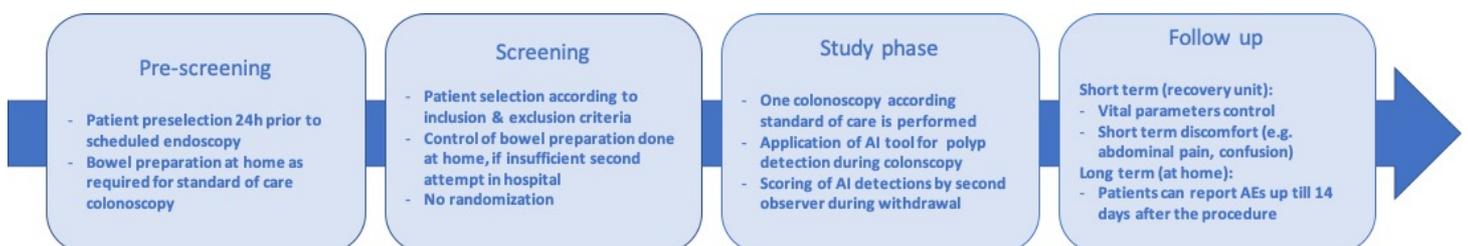
This study is an open label, unblinded, non-randomized interventional study, comparing the investigational artificial intelligence tool with the current “gold standard”: Data acquisition will be obtained during one scheduled colonoscopic procedure by a trained endoscopist. During insertion, no action will be taken, colonoscopy is performed following the standard of care. Once withdrawal is started, a second observer (not a trained endoscopist but person trained in polyp recognition) will start the bedside AI tool, connected to the endoscope’s tower, for detection. This second observer is trained in assessing endoscopic images to define the AI tool’s outcome. Due to the second observer watching the separate AI screen, the endoscopist is blinded of the AI outcome. When a detection is made by the AI system that is not recognized by the endoscopist, the endoscopist will be asked to relocate that same detection and to reassess the lesion and the possible need of therapeutic action. All detections are separately counted and categorized by the second observer. All polyp detections will be removed following standard of care for histological assessment. The entire colonoscopic procedure is recorded via a separate linked video-recorder.

Course of the study

Your participation in the study will involve only one colonoscopy, as scheduled, and no additional visits are involved in your care if you do not take part in the study.

Similarly, no additional examinations or procedures will be required in connection with the study (see details in appendix III.1.).

Since your participation in the study is part of the care of your clinical situation, all of the different phases we will describe are part of the normal care provided in your hospital.



- During the procedure a bedside module, consisting of a desktop computer and screen connected to the endoscope’s tower via the SDI output connection and linked to a video recorder, is used for polyp detection after image processing. No extra endoscopic equipment is necessary. The system is connectable to all endoscope systems (Pentax, Fuji, Olympus).

If you agree to take part in the study and meet all the conditions required to be enrolled in the study, you no extra tests or/and examinations are required.

Risks and discomforts

A: Medicine or other interactions

Contraindications:

- Any contraindication to undergo a standard colonoscopy or biopsy taken during colonoscopy
- Uncontrolled coagulopathy
- Pregnancy
- Recent (<2-4 weeks) colonic or ileocaecal surgery

Risks:

- Colonoscopy linked:
 - o Bleeding (post polypectomy)
 - o Colon perforation (post polypectomy)
 - o Post polypectomy syndrome (pain syndrome due to peritoneal inflammation after colonic transmural migration of the inflammation caused by electrocoagulation)
- AI linked:
 - o No additional risks to mention since the system only processes images made during colonoscopy

B: Side effects of the study medical device

The use of a separate, bedside AI tool that only processes real-time images makes the system independent of the endoscopy. Hence, no side-effects were reported in our previous pilot study in which we assessed the clinical use of this system. There are no side-effects from the AI tool itself to be expected.

C: Contraception, pregnancy and breast-feeding

Female participant: Because colonoscopy is only performed in (semi)urgent setting in pregnant women, you will not be allowed to take part in this clinical study if you are pregnant. Women who wish to become pregnant or are breast-feeding can safely be included without any risk for future pregnancies.

Male participant: There is a complete absence of risks for the partner of a male participant in the clinical study for a future pregnancy.

D: Risks associated with the evaluation procedures specific to the study

Since there are no specific examinations that will be performed in connection with this study, there is no extra risk for the participant than the risk of a standard of care colonoscopy.

Withdrawal from the study

Your participation is voluntary and you are entitled to withdraw from the study for any reason, without having to justify your decision. Nevertheless, it may be useful for the investigator and for the sponsor of the study to know if you are withdrawing because of the intervention itself.

It is also possible that the investigator withdraws you from the study because you are pregnant, because he/she thinks it is better for your health or because he/she finds out meet other exclusion criteria of this study.

Finally, the competent national or international authorities, the ethics committee that initially approved the study or the sponsor may break off the study because the information gathered shows that the investigational treatment is not effective (does not deliver a sufficient level of improvement in the health of the participants), the investigational treatment causes more side effects or more serious side effects than anticipated, or for any other reason, such as, for example, the decision to stop research and development of the investigational medicinal product.

Samples of biological material collected during the study

The sponsor of the study undertakes that the samples will only be used within the context defined in the section "Progress of clinical research" and its appendices.

If you take part in this clinical study, we ask you:

- To cooperate fully in the smooth running of this study.
- Not to conceal any information relating to your state of health, the medication you are taking or the symptoms you are experiencing.
- To carry the "emergency card" with you at all times, if applicable. This is imperative for your safety in the event of emergency care in an institution that does not know you.

You should also be aware that:

For your safety, it is advisable for your GP, if you have one, or other specialists in charge of your health to be informed of your participation in this study. We will ask you to confirm your agreement, but will respect your wish not to inform them where applicable.

Contact

If you need further information, but also if you have problems or concerns, you can contact the investigator Prof. dr. Raf Bisschops or a member of his research team on the following telephone number (016/34.21.61 or 016/34.19.46).

In case of emergency, you can contact Ms. Hilde Willekens on the following telephone number 016/34.03.96 or go straight to the nearest emergency unit.

Outside consulting hours, contact the A&E department of your hospital, indicating that you are taking part in a clinical study. Your records will contain information of use to the on-call doctor in relation to this clinical study.

If you have any questions relating to your rights as a participant in a clinical study, you can contact the patient rights ombudsman of your institution on this telephone number: 016/34.48.18. If necessary, he/she can put you in contact with the ethics committee.

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II Informed consent

Participant

I declare that I have been informed of the nature of the study, its purpose, its duration, any risks and benefits and what is expected of me. I have taken note of the information document and the appendices to this document.

I have had sufficient time to think about it and discuss it with a person of my choice, such as my GP or a member of my family.

I have had the opportunity to ask any questions that came to mind and have obtained a satisfactory response to my questions.

I understand that my participation in this study is voluntary and that I am free to end my participation in this study without this affecting my relationship with the therapeutic team in charge of my health.

I understand that data about me will be collected throughout my participation in this study and that the investigator and the sponsor of the study will guarantee the confidentiality of these data in accordance with applicable European and Belgian legislation. I understand that the performance of this study by UZ Leuven serves the general interest and that the processing of my personal data is necessary for the performance of this study.

I agree to my personal data being processed as described in the section dealing with confidentiality guarantees (appendix III.3, p 9/11). I also consent to these data being transferred to and processed in countries other than Belgium.

I agree to the study data collected for the purposes of this study being processed at a later date provided this processing is limited to the context of the present study for a better understanding of the disease and its treatment.

I agree to the sponsor retaining samples of biological material collected during the study for 10 years for subsequent research purposes but limited to the context of the present study.

I agree to my GP or other specialists in charge of my health being informed of my participation in this clinical study.

I have received a copy of the information to the participant and the informed consent form.

Surname, first name, date and signature of the volunteer.

Legal representative

I declare that I have been informed that I am being asked to take a decision on whether or not to take part in the clinical study for the person I represent in his/her best interests and taking into consideration his/her likely wishes. My consent applies to all the items listed in the consent of the participant.

I have received a copy of the information to the participant and the informed consent form.

Surname, first name and relationship to the person represented:

Date and signature of the legal representative.

Witness/Interpreter

I was present during the entire process of informing the patient and I confirm that the information on the objectives and procedures of the study was adequately provided, that the participant (or his/her legal representative) apparently understood the study and that consent to participate in the study was freely given.

Surname, first name and qualification of the witness/interpreter:

Date and signature of the witness/interpreter.

Investigator

I, the undersigned, Prof. dr. Raf Bisschops, investigator, or his clinical study assistant confirm that I have verbally provided the necessary information about the study and have given the participant a copy of the information document.

I confirm that no pressure was applied to persuade the patient to agree to take part in the study and that I am willing to answer any additional questions if required.

I confirm that I operate in accordance with the ethical principles set out in the latest version of the "Helsinki Declaration", the "Good Clinical Practices" and the Belgian Law of 7 May 2004 related to experiments on humans.

Surname, first name, date and signature
of the investigator's representative

Surname, first name, date and signature
of the investigator

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III Supplementary information

1: Supplementary information on the organisation of the study

This is an investigator-initiated non-randomized prospective interventional trial to validate the performance of a novel state-of-the-art computer-aided detection (CADe) tool for colorectal polyp detection implemented as second observer during routine diagnostic colonoscopy and to evaluate its feasibility in daily endoscopy. Consecutive patients referred for a screening, surveillance or diagnostic colonoscopy will be included.

Patients will undergo a standard colonoscopy performed by a trained endoscopist. A second observer, who is not a trained endoscopist, will follow the procedure on a bedside AI-tool to count the number of detections made by the AI system and categorize the results into positive or negative results as follows (1) true positive, (2) false negative or (3) false positive. In case of a detection of the AI-system that was not seen by the endoscopist or unclear to the second observer, the second observer will ask to re-evaluate the indicated region to determine whether after second look the endoscopist has to take extra action. The entire procedure will be recorded.

There are no additional risks specific to the use of the AI tool to be taken into account. General risk of colonoscopy (i.e.: perforation, bleeding or post-polypectomy syndrome) could occur with the same frequency as that of a colonoscopy without the use of this AI tool.

All patients will receive a standard of care protocol during their colonoscopy. The AI system can only have a beneficial outcome for the patient, a better polyp detection, as it has shown to be non-inferior in terms of accuracy when compared to high detecting endoscopist in our pilot trial.

2: Supplementary information on the risks associated with participation in the study

Our study is designed to test a “add-on intervention” of routine colonoscopy. Besides the general risks of a colonoscopy +/- polypectomy (bleeding, perforation, post-polypectomy syndrome) or side-effects (flatulence, abdominal pain or cramps, bloating) and those of sedatives/general anaesthetics (confusion, amnesia, nausea), the tested AI system itself has no additional risks or side effects for the patient. Moreover, it may provide a beneficial effect for the patient, a better polyp detection.

3: Supplementary information on the protection and the rights of the participant in a clinical study

Ethics Committee

This study has been reviewed by an independent Ethics Committee, namely the Ethics Committee of Research UZ/KU Leuven, which has issued a favourable opinion. It is the task of the Ethics Committees to protect people who take part in a clinical trial. They make sure that your rights as a patient and as a participant in a clinical study are respected, that based on current knowledge, the balance between risks and benefits remains favourable to the participants, that the study is scientifically relevant and ethical.

You should not under any circumstances take the favourable opinion of the Ethics Committee as an incentive to take part in this study.

Voluntary participation

Before signing, do not hesitate to ask any questions you feel are appropriate. Take the time to discuss matters with a trusted person if you so wish.

Your participation in the study is voluntary and must remain free of any coercion: this means that you have the right not to take part in the study or to withdraw without giving a reason, even if you previously agreed to take part. Your decision will not affect your relationship with the investigator or the quality of your future therapeutic care.

However, it is advisable for your safety to inform the investigator if you have decided to stop taking part in the study.

If you agree to take part, you will sign the informed consent form. The investigator will also sign this form to confirm that he/she has provided you with the necessary information about the study. You will receive a copy of the form.

Guarantee of confidentiality

Your participation in the study means that your personal data are collected by the investigator and used in an encoded form by the study sponsor for research purposes and in connection with scientific and medical publications.

The processing of your personal data is necessary to achieve the scientific research purposes as set out herein. The conduct of scientific research is one of the core missions of UZ Leuven as defined by law. As a university hospital, part of KU Leuven, UZ Leuven is indeed required to support research and education in the public interest. We would therefore like to inform you that the necessity of the processing for the conduct of scientific research as a task of public interest constitutes the lawful basis on which we process your information in the context of the study in which you are participating. UZ Leuven is also subject to specific legal requirements which require the processing of your personal in the context of safety reporting (such as for example the notification of adverse events to the regulatory authorities).

Your data will be processed in accordance with the European General Data Protection Regulation (GDPR). University Hospitals Leuven shall act as data controller for your data. You are entitled to ask the investigator what data are being collected about you and what is their use in connection with the study. This data concerns your current clinical situation but also some of your background, the results of examinations carried out within the context of care of your health in accordance with the current

standards and obviously the results of examinations required by the protocol. You have the right to inspect these data and correct them if they are incorrect¹.

The investigator has a duty of confidentiality vis-à-vis the data collected.

This means that he/she undertakes not only never to reveal your name in the context of a publication or conference but also that he/she will encode (your identity will be replaced by an ID code in the study) your data before sending them to the manager of the database of collected data (Department of Gastroenterology and Hepatology, Endoscopy Unit, University Hospitals Leuven, Herestraat 49, B-3000 Leuven).

The investigator and his/her team will therefore be the only ones to be able to establish a link between the data transmitted throughout the study and your medical records².

The personal data transmitted will not contain any combination of elements that might allow you to be identified³.

For the study data manager designated by the sponsor, the data transmitted will not allow you to be identified. The latter is responsible for collecting the data gathered by all investigators taking part in the study, processing them and protecting them in accordance with the requirements of the Belgian law on the protection of privacy.

To verify the quality of the study, it is possible that your medical records will be examined by persons subject to professional secrecy and designated by the ethics committee, the sponsor of the study or an independent audit body. In any event, this examination of your medical records may only take place under the responsibility of the investigator and under the supervision of one of the collaborators designated by him/her.

The (encoded) study data will be able to be sent to Belgian or other regulatory authorities, to the relevant ethics committees, to other doctors and/or to organisations working in collaboration with the sponsor.

They will also be able to be sent to other sites of the sponsor in Belgium and in other countries where the standards in terms of the protection of personal data may be different or less stringent? As explained above, the transmitted data are encoded⁴.

Your consent to take part in this study therefore also implies your consent to the use of your encoded medical data for the purposes described in this information form and to their transmission to the aforementioned people and authorities.

The sponsor undertakes only to use the data collected within the context of the study in which you are taking part.

If you withdraw your consent to take part in the study, to guarantee the validity of the research, the data encoded up to the point at which you withdraw will be retained. No new data may be sent to the sponsor.

If you have any questions relating to how your data are being processed, you may contact the investigator. The data protection officer in your hospital can be contacted as well: DPO - UZ Leuven, Herestraat 49, 3000 Leuven, e-mail dpo@uzleuven.be.

Finally, if you have a complaint concerning the processing of your data, you can contact the Belgian supervisory authority who ensures that privacy is respected when personal data are processed.

The Belgian supervisory authority is called:
Data Protection Authority (DPA)
Drukpersstraat 35,
1000 Brussels

¹ These rights are guaranteed by the European Data Protection Regulation (GDPR) and by the Law of 22 August 2002 on patient rights.

² For clinical trials, the law requires this link with your records to be retained for 20 years. In the case of a advanced therapy medicinal product using human biological material, this period will be a minimum of 30 years and a maximum of 50 years in accordance with the Belgian Law of 19 December 2008 on the use of human biological material and the applicable royal decrees.

³ The database containing the results of the study will therefore not contain any combination of elements such as your initials, your gender and your full date of birth (dd/mm/yyyy).

⁴ The sponsor then undertakes to respect the constraints of the European General Data Protection Regulation (GDPR) and the Belgian legislation on the protection of natural persons with regard to the processing of personal data.

Tel. +32 2 274 48 00
e-mail: contact@apd-gba.be
Website: <https://www.dataprotectionauthority.be>

Future of your sample(s) collected during the study

The sample encoding procedure is the same as that used for your medical data. Samples sent to the sponsor will therefore only include your study ID code.

The manager of these samples (Department of Anatomopathology, University Hospitals Leuven, Herestraat 49, B-3000 Leuven) undertakes to use them within the context of clinical research and to destroy them at the end of the scheduled storage period.

The sample of biological material taken is deemed to be a “donation” and you should be aware that, in principle, you will not receive any financial benefit (royalties) associated with the development of new therapies derived from the use of your donation of biological material and which may be of commercial value.

If you withdraw your consent to take part in the study, you may contact the investigator and have those of your samples that have not yet been used destroyed. The results obtained from your samples before you withdraw your consent remain the property of the study sponsor.

Insurance

Any participation in a clinical study involves a risk, however small it is. Even if there is no fault, the sponsor accepts responsibility for damage caused to the participant (or in the event of death, his/her dependants) and directly or indirectly linked to his/her participation in the study. The sponsor has taken out insurance for this responsibility⁵.

You are therefore asked to report any new health problem to the investigator. He/she will be able to provide you with additional information concerning possible treatments.

If the investigator believes that a link with the study is possible (the insurance does not cover the natural progression of your disease or the known side effects of your normal treatment), he/she will inform the study sponsor, which will initiate the declaration procedure to the insurance company. The latter will appoint an expert - if it considers it necessary - to assess whether there is a link between your new health problems and the study.

In the event of disagreement either with the investigator or with the expert appointed by the insurance company and also whenever you feel it is appropriate, you or - in case of death - your dependants may bring proceedings against the insurer directly in Belgium (Amlin Corporate Insurance, policy number. 299.053.700, contact details: Vanbreda Risk & Benefits, Plantin en Moretuslei 297, 2140 Antwerp).

The law provides that the insurer may be summoned to appear either before the judge of the location where the event giving rise to the damage occurred, or before the judge of your domicile, or before the judge of the insurer's registered offices.

⁵ In accordance with Article 29 of the Belgian Law related to experiments on humans (7 May 2004)